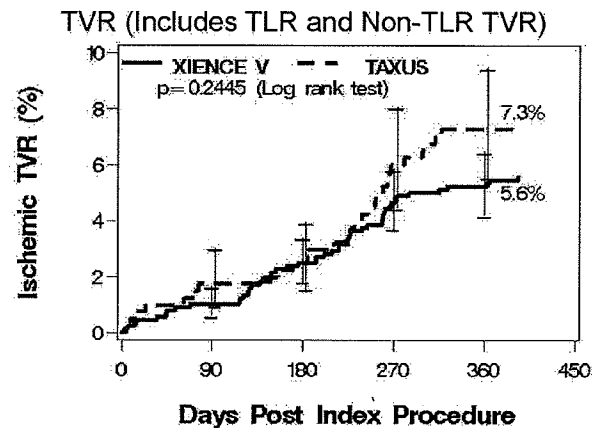
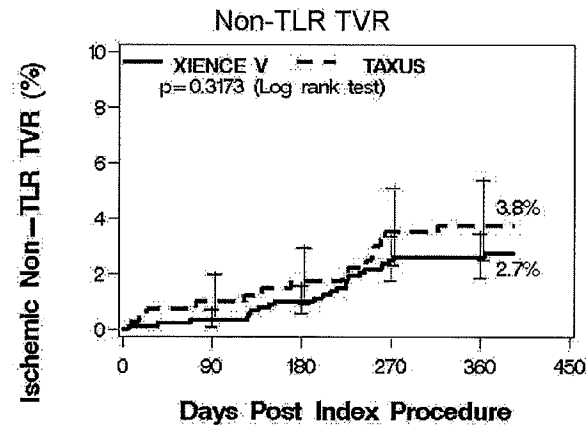


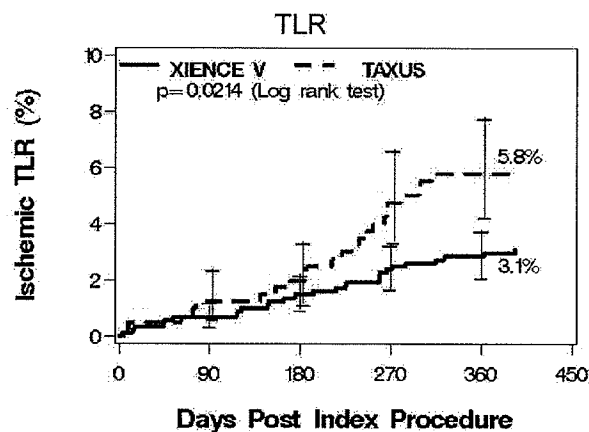
**Figure 9.4-1: Kaplan Meier Hazard Curves for Time to First TVR or TLR Event through 393 Days (Pooled SPIRIT II and SPIRIT III RCTs)**



Note: P-value is not adjusted for multiplicity and is meant for descriptive purposes only.



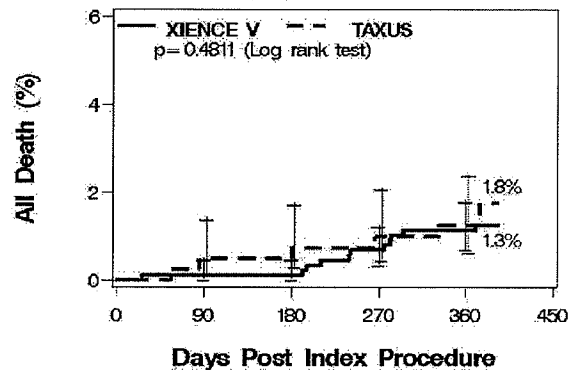
Note: P-value is not adjusted for multiplicity and is meant for descriptive purposes only.



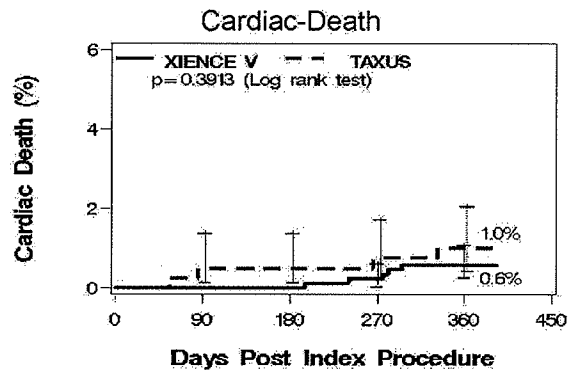
Note: P-value is not adjusted for multiplicity and is meant for descriptive purposes only.

Pooled analyses of the rates of all death, cardiac death, and non-cardiac death through 1 year are shown in Figure 9.4-2.

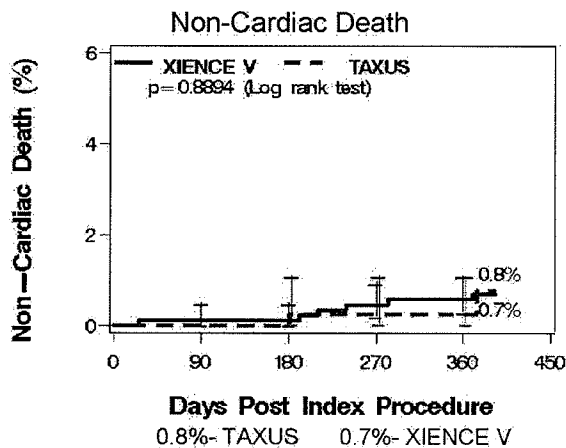
**Figure 9.4-2: Kaplan Meier Hazard Curves for Time to Death through 393 Days  
(Pooled SPIRIT II and SPIRIT III RCTs)  
All Death**



Note: P-value is not adjusted for multiplicity and is meant for descriptive purposes only.



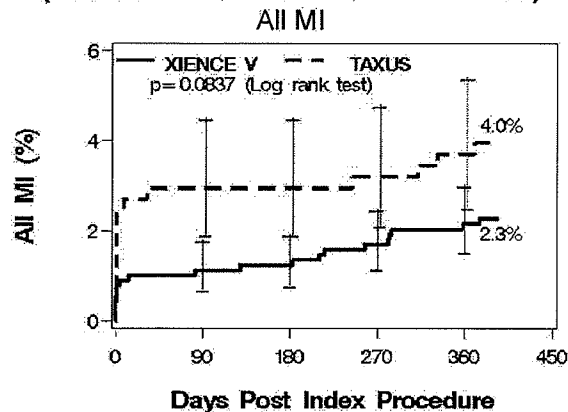
Note: P-value is not adjusted for multiplicity and is meant for descriptive purposes only.



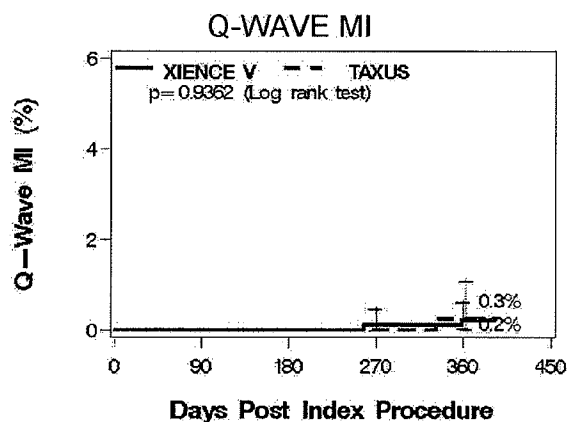
Note: P-value is not adjusted for multiplicity and is meant for descriptive purposes only.

Pooled analyses of the rates of MIs through 1 year are shown in Figure 9.4-3.

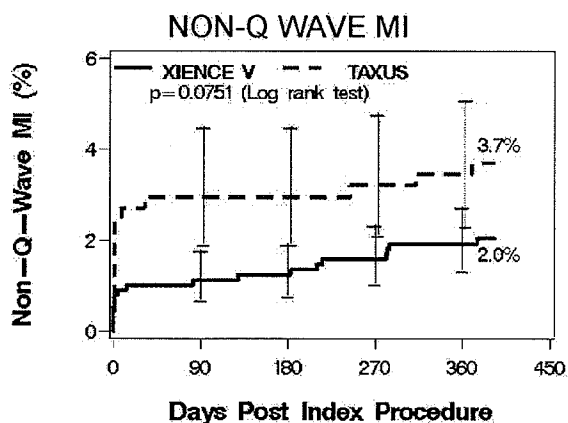
**Figure 9.4-3: Kaplan Meier Hazard Curves for Time to First MI Event through 393 Days (Pooled SPIRIT II and SPIRIT III RCTs)**



Note: P-value is not adjusted for multiplicity and is meant for descriptive purposes only.



Note: P-value is not adjusted for multiplicity and is meant for descriptive purposes only.



Note: P-value is not adjusted for multiplicity and is meant for descriptive purposes only.

### 9.4.1 Stent Thrombosis in SPIRIT II and SPIRIT III Pooled Analysis

The results for the pooled analysis rates of stent thrombosis at one year are shown below in Figure 9.4.1-1. Rates were low for both treatments in this pooled analysis and consistent with the published literature<sup>10</sup>. The rates of stent thrombosis were evaluated based on the SPIRIT II and III protocol defined definition and the ARC definition for definite + probable thrombosis (see definitions above in Section 8.2). These data are presented in table 9.4.1-1.

**Table 9.4.1-1 Pooled Results for Stent Thrombosis through 1 year  
(SPIRIT II and SPIRIT III RCT)**

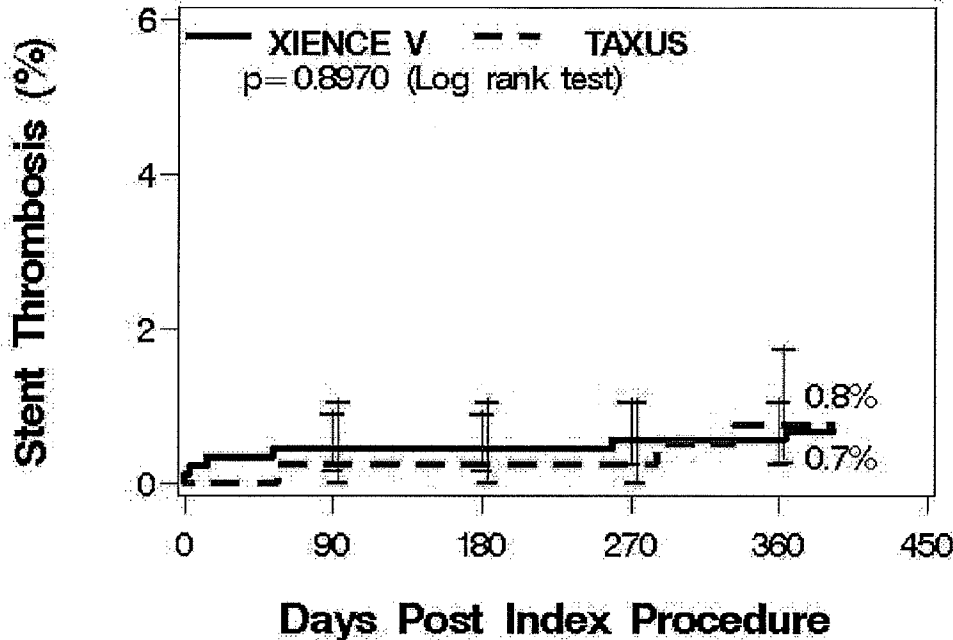
	XIENCE V (N=892)	95% CI <sup>1</sup>	TAXUS (N=410)	95% CI <sup>1</sup>
<b>0 - 30 days</b>				
Protocol	0.3% (3/890)	[0.07%, 0.98%]	0.0% (0/407)	[0.00%, 0.90%]
ARC (definite + probable)	0.4% (4/890)	[0.12%, 1.15%]	0.2% (1/407)	[0.01%, 1.36%]
<b>31 days – 1 year</b>				
Protocol	0.3% (3/866)	[0.07%, 1.01%]	0.8% (3/394)	[0.16%, 2.21%]
ARC (definite + probable)	0.3% (3/867)	[0.07%, 1.01%]	0.8% (3/394)	[0.16%, 2.21%]
<b>0 – 1 year</b>				
Protocol	0.7% (6/867)	[0.25%, 1.50%]	0.8% (3/394)	[0.16%, 2.21%]
ARC (definite + probable)	0.8% (7/868)	[0.32%, 1.65%]	0.8% (3/394)	[0.16%, 2.21%]

Note: timeframe for 1 year includes the follow-up window (365 + 28 days)  
<sup>1</sup> By Clopper-Pearson Exact Confidence Interval

<sup>10</sup> Ellis SG CA, Grube E, Popma J, Koglin J, Dawkins KD, Stone GW. Incidence, timing, and correlates of stent thrombosis with the polymeric paclitaxel drug-eluting stent: a TAXUS II, IV, V, and VI meta-analysis of 3,445 patients followed for up to 3 years. *J Am Coll Cardiol*. 2007;49:1043-1051.

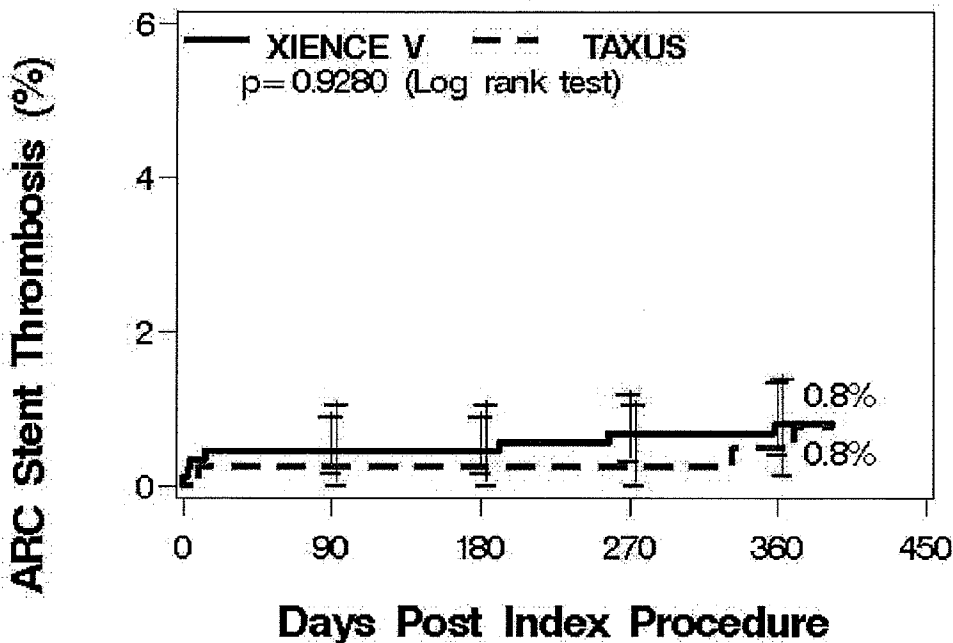
**Figure 9.4.1-1: Kaplan Meier Hazard Curves for Time to First Stent Thrombosis Event through 393 Days (Pooled SPIRIT II and SPIRIT III RCTs)**

Protocol Defined Stent Thrombosis



Note: P-value is not adjusted for multiplicity and is meant for descriptive purposes only.

ARC DEFINED STENT THROMBOSIS (DEFINITE + PROBABLE)



Note: P-value is not adjusted for multiplicity and is meant for descriptive purposes only.

### 9.4.2 Diabetics in SPIRIT II and SPIRIT III Pooled Analysis

Diabetic subjects comprise an important subject subgroup that is at increased risk for cardiovascular morbidity and mortality. Although diabetic subjects were included in the SPIRIT family of trials, there were no pre-specified hypotheses or trial features that warrant a specific labeled indication for the use of the XIENCE V stent in diabetic individuals.

Table 9.4.2-1 shows the clinical outcomes through 1 year in subjects pooled from SPIRIT II and III. The randomization was stratified by history of diabetes to assure a balance between the XIENCE V and TAXUS treatment arms. In XIENCE V patients, there were numerically higher event rates in diabetics compared with non-diabetics. The event rates for TAXUS in diabetics were lower than the event rates for TAXUS non-diabetics. Given the relatively small sample size of the diabetic population and potential for confounding variables, no conclusions can be drawn from these post-hoc analyses.

**Table 9.4.2-1: Clinical Results in Diabetics and Non-Diabetics through 1 year  
(SPIRIT II and SPIRIT III RCT Pooled Population)**

	Non-Diabetics XIENCE V (N=643)	Non-Diabetics TAXUS (N=296)	All Diabetics XIENCE V (N=249)	All Diabetics TAXUS (N=110)
TLR	2.5% (16/629)	7.6% (22/290)	4.5% (11/244)	1.0% (1/104)
TVR(CABG/PCI), non TL	2.5% (16/629)	4.1% (12/290)	3.3% (8/244)	2.9% (3/104)
All Death	1.0% (6/631)	2.4% (7/291)	2.0% (5/246)	0.0% (0/104)
Cardiac Death	0.3% (2/631)	1.4% (4/291)	1.2% (3/246)	0.0% (0/104)
Non-Cardiac Death	0.6% (4/631)	1.0% (3/291)	0.8% (2/246)	0.0% (0/104)
MI	1.4% (9/629)	4.5% (13/290)	4.5% (11/244)	2.9% (3/104)
Cardiac Death or MI	1.7% (11/629)	5.2% (15/290)	5.3% (13/244)	2.9% (3/104)
Stent Thrombosis				
Protocol defined	0.5% (3/627)	1.0% (3/287)	1.3% (3/240)	0.0% (0/104)
ARC definite + probable	0.3% (2/627)	0.7% (2/287)	2.1% (5/241)	1.0% (1/104)

**Table 9.4.2-2: Clinical Results in Diabetics through 1 year  
(SPIRIT II and SPIRIT III RCT Pooled Population – XIENCE V Subjects)**

	Non-Diabetics (N=643)	All Diabetics (N=249)	Insulin-Dependent Diabetics (N=63)	Non-Insulin-Dependent Diabetics (N=186)
TLR	2.5% (16/629)	4.5% (11/244)	6.5% (4/62)	3.8% (7/182)
TVR(CABG/PCI), non TL	2.5% (16/629)	3.3% (8/244)	1.6% (1/62)	3.8% (7/182)
All Death	1.0% (6/631)	2.0% (5/246)	3.2% (2/63)	1.6% (3/183)
Cardiac Death	0.3% (2/631)	1.2% (3/246)	1.6% (1/63)	1.1% (2/183)
Non-Cardiac Death	0.6% (4/631)	0.8% (2/246)	1.6% (1/63)	0.5% (1/183)
MI	1.4% (9/629)	4.5% (11/244)	9.7% (6/62)	2.7% (5/182)
Cardiac Death or MI	1.7% (11/629)	5.3% (13/244)	9.7% (6/62)	3.8% (7/182)
Stent Thrombosis				
Protocol defined	0.5% (3/627)	1.3% (3/240)	1.6% (1/61)	1.1% (2/179)
ARC definite + probable	0.3% (2/627)	2.1% (5/241)	1.6% (1/61)	2.2% (4/180)

#### 9.4.3 Dual Vessel treatment in SPIRIT II and SPIRIT III Pooled Analysis

Subjects requiring treatment in more than one vessel comprise a subgroup that is at increased risk for cardiovascular events compared with single vessel disease patients. Although subjects requiring both single and dual vessel treatment were included in the SPIRIT family of trials, there were no pre-specified hypothesis or trial features that warrant a specific labeled indication for the use of the XIENCE V stent in dual vessel individuals.

Table 9.4.3-1 shows the clinical outcomes through 1 year in subjects pooled from SPIRIT II and III. The randomization was stratified by the number of vessels treated to assure a balance between the XIENCE V and TAXUS treatment arms. Numerically lower event rates were observed for XIENCE V and TAXUS in single compared to dual vessel treatment. However, given the small sample size for dual vessel treatment, no conclusions can be drawn from this post-hoc analysis.

**Table 9.4.3-1: Clinical Results in Single and Dual Vessel Treatment through 1 year  
(SPIRIT II and SPIRIT III RCT Pooled Population)**

	Single Vessel XIENCE V (N=752)	Single Vessel TAXUS (N=344)	Dual Vessel XIENCE V (N=140)	Dual Vessel TAXUS (N=65)
TLR	2.9% (21/735)	4.5% (15/333)	4.3% (6/138)	12.5% (8/64)
TVR(CABG/PCI), non TLR	2.3% (17/735)	2.1% (7/333)	5.1% (7/138)	12.5% (8/64)
All Death	1.5% (11/739)	1.2% (4/333)	0.0% (0/138)	4.6% (3/65)
Cardiac Death	0.7% (5/739)	0.6% (2/333)	0.0% (0/138)	3.1% (2/65)
Non-Cardiac Death	0.8% (6/739)	0.6% (2/333)	0.0% (0/138)	1.5% (1/65)

	Single Vessel XIENCE V (N=752)	Single Vessel TAXUS (N=344)	Dual Vessel XIENCE V (N=140)	Dual Vessel TAXUS (N=65)
MI	1.9% (14/735)	3.0% (10/333)	4.3% (6/138)	9.4% (6/64)
Cardiac Death or MI	2.4% (18/735)	3.3% (11/333)	4.3% (6/138)	10.9% (7/64)
Stent Thrombosis				
Protocol defined	0.3% (2/729)	0.6% (2/332)	2.9% (4/138)	1.6% (1/62)
ARC definite + probable	0.5% (4/730)	0.6% (2/332)	2.2% (3/138)	1.6% (1/62)

## 10.0 INDIVIDUALIZATION OF TREATMENT

The risks and benefits should be considered for each patient before using the PROMUS stent. Patient selection factors to be assessed should include a judgment regarding risk of long-term antiplatelet therapy. Stenting is generally avoided in those patients at a heightened risk of bleeding (e.g., patients with recently active gastritis or peptic ulcer disease) in which anticoagulation therapy would be contraindicated.

Antiplatelet drugs should be used in combination with the PROMUS stent. Physicians should use information from the SPIRIT Clinical trials, coupled with current drug eluting stent (DES) literature and the specific needs of individual patients to determine the specific antiplatelet/anticoagulation regimen to be used for their patients in general practice. See also 5.2 – Precautions, Pre- and Post-Procedure Antiplatelet Regimen, Section 5.6 – Precautions, Use in Special Populations and Section 5.7 – Precautions, Lesion/Vessel Characteristics.

Premorbid conditions that increase the risk of poor initial results or the risks of emergency referral for bypass surgery (diabetes mellitus, renal failure, and severe obesity) should be reviewed.

## 11.0 PATIENT COUNSELING AND PATIENT INFORMATION

Physicians should consider the following in counseling patients about this product:

- Discuss the risks associated with stent placement.
- Discuss the risks associated with an everolimus-eluting stent.
- Discuss the risks of early discontinuation of the antiplatelet therapy.
- Discuss the risks of late stent thrombosis with DES use in higher risk patient subgroups.
- Discuss the risk/benefit issues for this particular patient.
- Discuss alteration to current life-style immediately following the procedure and over the long term.

The following patient materials are available for this product:

- A Patient Information Guide which includes information on coronary artery disease, the implant procedure and the PROMUS Everolimus-Eluting Coronary Stent System (provided to physician, on-line at [www.bostonscientific.com/promus](http://www.bostonscientific.com/promus), or by calling customer service 1-888-272-1001).
- A Stent Implant Card that includes both patient information and stent implant information (provided in package)

## 12.0 HOW SUPPLIED

**Sterile:** This device is sterilized with ethylene oxide gas, non-pyrogenic. It is intended for single use only. Do not resterilize. Do not use if the package is opened or damaged.

**Contents:** One (1) PROMUS Everolimus-Eluting Coronary Stent System, one (1) Flushing tool, (for the PROMUS EECSS Rapid Exchange (RX) Stent System), one (1) Stent Implant Card, one (1) Patient Information Guide.

**Storage:** Store in a dry, dark, cool place. Protect from light. Do not remove from carton until ready for use. Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).

## 13.0 OPERATOR'S INSTRUCTIONS

### 13.1 Inspection Prior to Use

- Carefully inspect the sterile package before opening and check for damage to the sterile barrier. Do not use if the integrity of the sterile package has been compromised.
- Do not use after the "Use By" date.
- Tear open the foil pouch and remove the inner pouch. **Note: the outside of the inner pouch is NOT sterile.** Open the inner pouch and pass or drop the product into the sterile field using an aseptic technique.
- Prior to using the PROMUS Everolimus-Eluting Coronary Stent System, carefully remove the system from the package and inspect for bends, kinks, and other damage. Verify that the stent does not extend beyond the radiopaque balloon markers. Do not use if any defects are noted. However, **do not manipulate, touch, or handle the stent** with your fingers, which may cause coating damage, contamination or stent dislodgement from the delivery balloon.

**Note:** At any time during use of the PROMUS Rapid Exchange (RX) EECSS, if the stainless steel proximal shaft has been bent or kinked, do not continue to use the catheter.

### 13.2 Materials Required

- Appropriate guiding catheter(s). See Table 1-1, PROMUS Stent System Product Description
- 2 – 3 syringes (10 – 20 ml)
- 1,000 u/500 ml Heparinized Normal Saline (HepNS)
- 0.014 inch (0.36 mm) x 175 cm (minimum length) guide wire
- Rotating hemostatic valve with appropriate minimum inner diameter [0.096 inch (2.44 mm)]
- 60% contrast diluted 1:1 with heparinized normal saline
- Inflation device

- Pre-deployment dilatation catheter
- Three-way stopcock
- Torque device
- Guide wire introducer
- Appropriate arterial sheath
- Appropriate anticoagulation and antiplatelet drugs

### 13.3 Preparation

#### 13.3.1 Packaging Removal

**Note: The foil pouch is not a sterile barrier.** The inner header bag (pouch) within the foil pouch is the sterile barrier. Only the contents of the inner pouch should be considered sterile. The outside surface of the inner pouch is NOT sterile.

1. Carefully remove the delivery system from its protective tubing for preparation of the delivery system. When using a Rapid Exchange (RX) system, do not bend or kink the hypotube during removal.
2. Remove the product mandrel and protective stent sheath by grasping the catheter just proximal to the stent (at the proximal balloon bond site), and with the other hand, grasp the stent protector and gently remove distally. If unusual resistance is felt during product mandrel and stent sheath removal, do not use this product and replace with another. Follow product returns procedure for the unused device.

#### 13.3.2 Guide Wire Lumen Flush

1. Over the Wire (OTW) only: Flush the guide wire lumen with HepNS until fluid exits the distal end of the delivery system.
2. Rapid Exchange (RX) only: Flush the guide wire lumen with HepNS using the flushing tool supplied with the product. Insert the flushing tool into the tip of the catheter and flush until fluid exits the guide wire exit notch.

**Note:** Avoid manipulation of the stent while flushing the guide wire lumen, as this may disrupt the placement of the stent on the balloon.

### 13.3.3 Delivery System Preparation

1. Prepare an inflation device/syringe with diluted contrast medium.
2. Attach an inflation device/syringe to the stopcock; attach it to the inflation port of the product. Do not bend the product hypotube when connecting to the inflation device/syringe.
3. With the tip down, orient the delivery system vertically.
4. Open the stopcock to delivery system; pull negative for 30 seconds; release to neutral for contrast fill.
5. Close the stopcock to the delivery system; purge the inflation device/syringe of all air.
6. Repeat steps 3 through 5 until all air is expelled. If bubbles persist, do not use the product.
7. If a syringe was used, attach a prepared inflation device to stopcock.
8. Open the stopcock to the delivery system.
9. Leave on neutral

**Note:** If air is seen in the shaft, repeat Delivery System Preparation steps 3 through 5 to prevent uneven stent expansion.

### 13.4 Delivery Procedure

1. Prepare the vascular access site according to standard practice.
2. **Pre-dilate the lesion with a PTCA catheter of appropriate length and diameter for the vessel/lesion to be treated.** Limit the longitudinal length of pre-dilatation by the PTCA balloon to avoid creating a region of vessel injury that is outside the boundaries of the PROMUS Stent.

**Note:** The labeled stent diameter refers to expanded stent inner diameter.

3. Maintain neutral pressure on the inflation device attached to the delivery system. Open the rotating hemostatic valve as wide as possible.
4. Backload the delivery system onto the proximal portion of the guide wire while maintaining guide wire position across the target lesion.
5. Carefully advance the delivery system into the guiding catheter and over the guide wire to the target lesion. When using a Rapid Exchange (RX) system be sure to keep the hypotube straight. Ensure guiding catheter stability before advancing the stent system into the coronary artery.

**Note:** If unusual resistance is felt before the stent exits the guiding catheter, do not force passage. Resistance may indicate a problem and the use of excessive force may result in stent damage or dislodgement. Maintain guide wire placement across the lesion and remove the delivery system and guiding catheter as a single unit.

6. Advance the delivery system over the guide wire to the target lesion under direct fluoroscopic visualization. Utilize the radiopaque balloon markers to position the stent across the lesion. Perform angiography to confirm stent position. If the position of the stent is not optimal, it should be carefully repositioned or removed (see Section 5.14 – Precautions, Delivery System Removal). The balloon markers indicate both the stent edges and the balloon shoulders. Expansion of the stent should not be undertaken if the stent is not properly positioned in the target lesion.

**Note:** Should **any resistance** be felt at any time during either lesion access or removal of the delivery system post-stent implantation, **remove the entire system as a single unit.** See Section 5.14 – Precautions, Delivery System Removal for specific delivery system removal instructions.

7. Tighten the rotating hemostatic valve. The stent is now ready to be deployed.

### 13.5 Deployment Procedure

**CAUTION:** Refer to Table 14-1: Typical PROMUS Stent Compliance for in vitro stent inner diameter, nominal pressure, and RBP.

1. Prior to deployment, reconfirm the correct position of the stent relative to the target lesion using the radiopaque balloon markers.
2. Deploy the stent slowly by pressurizing the delivery system in 2 atm increments, every 5 seconds, until stent is completely expanded. Accepted practice generally targets an initial deployment pressure that would achieve a stent inner diameter ratio of about 1.1 times the reference vessel diameter (see Table 14-1). Maintain pressure for 30 seconds. If necessary, the delivery system can be repressurized or further pressurized to assure complete apposition of the stent to the artery wall. **Do not exceed the labeled rated burst pressure (RBP) of 16 atm (1.62 MPa).**
3. Fully cover the entire lesion and balloon treated area (including dissections) with the PROMUS stent, allowing for adequate stent coverage into healthy tissue proximal and distal to the lesion.
4. Deflate the balloon by pulling negative on the inflation device for 30 seconds. Confirm complete balloon deflation before attempting to move the delivery system. If unusual resistance is felt during stent delivery system withdrawal, pay particular attention to guiding catheter position.
5. Confirm stent position and deployment using standard angiographic techniques. For optimal results, the entire stenosed arterial segment should be covered by the stent. Fluoroscopic visualization during stent expansion should be used in order to properly judge the optimum expanded stent diameter as compared to the proximal and distal coronary artery diameter(s). Optimal expansion requires that the stent be in full contact with the artery wall. Stent wall contact should be verified through routine angiography or intravascular ultrasound (IVUS).
6. If the deployed stent size is still inadequate with respect to reference vessel diameter, a larger balloon may be used to further expand the stent. If the initial angiographic appearance is sub-optimal, the stent may be further expanded using a low profile, high pressure, non-compliant balloon dilatation catheter. If this is required, the stented segment should be carefully recrossed with a prolapsed guide wire to avoid disrupting the stent geometry. Deployed stents should not be left under-dilated.

**CAUTION:** Do not dilate the stent beyond the following limits.

<u>Nominal Stent Diameter</u>	<u>Dilatation Limit</u>
2.5 mm to 3.0 mm	3.5 mm
3.5 mm to 4.0 mm	4.5 mm

7. If more than one PROMUS stent is needed to cover the lesion and balloon treated area, it is suggested that, to avoid the potential for gap restenosis, the stents be adequately overlapped. To ensure that there are no gaps between

stents the balloon marker bands of the second PROMUS stent should be positioned inside the deployed stent prior to expansion.

8. Reconfirm stent position and angiographic results. Repeat inflations until optimal stent deployment is achieved.

### 13.6 Removal Procedure

1. Deflate the balloon by pulling negative pressure on the inflation device for 30 seconds. Confirm complete balloon deflation before attempting to move the delivery system. If unusual resistance is felt during stent delivery system withdrawal, pay particular attention to the guiding catheter position.
2. Fully open the rotating hemostatic valve.
3. While maintaining the guide wire position and negative pressure on the inflation device, withdraw the delivery system.

**Note:** Should any resistance be felt at any time during either lesion access or removal of the delivery system post-stent implantation, the entire system should be **removed as a single unit**. See Section 5.14 – Precautions, Delivery System Removal for specific delivery system removal instructions.

4. Tighten the rotating hemostatic valve.
5. Repeat angiography to assess the stented area. If post-dilatation is necessary, ensure that the final stent diameter matches the reference vessel diameter.  
**Assure that the stent is not under-dilated.**

### 13.7 Post-Deployment Dilatation of Stent Segments

1. All efforts should be taken to assure that the stent is not underdilated. If the deployed stent size is still inadequate with respect to the vessel diameter, or if full contact with the vessel wall is not achieved, a larger balloon may be used to expand the stent further. The stent may be further expanded using a low profile, high pressure, and non-compliant balloon catheter. If this is required, the stented segment should be recrossed carefully with a prolapsed guide wire to avoid dislodging the stent. The balloon should be centered within the stent and should not extend outside of the stented region.

**CAUTION:** Do not dilate the stent beyond the following limits.

<u>Nominal Stent Diameter</u>	<u>Dilatation Limit</u>
2.5 mm to 3.0 mm	3.5 mm
3.5 mm to 4.0 mm	4.5 mm

**14.0 IN VITRO COMPLIANCE INFORMATION**

**Table 14-1: Typical PROMUS Stent Compliance**  
Nominal pressure for each diameter indicated by bold font.

Pressure		Stent ID (mm) by System Size				
(atm)	(MPa)	2.5 mm	2.75 mm	3.0 mm	3.5 mm	4.0 mm
8	0.81	<b>2.46</b>	<b>2.74</b>	2.90	3.46	3.86
9	0.91	2.52	2.81	<b>2.97</b>	<b>3.55</b>	<b>3.95</b>
10	1.01	2.58	2.87	3.04	3.63	4.03
11	1.11	2.63	2.92	3.10	3.69	4.10
12	1.22	2.68	2.97	3.15	3.75	4.17
13	1.32	2.72	3.01	3.19	3.80	4.23
14	1.42	2.75	3.05	3.23	3.84	4.28
15	1.52	2.78	3.08	3.26	3.89	4.33
16 (RBP)*	1.62	2.81	3.11	3.30	3.93	4.37
17	1.72	2.84	3.14	3.33	3.97	4.42
18	1.82	2.87	3.18	3.36	4.00	4.46

Note: These nominal data are based on *in vitro* testing at 37°C and do not take into account lesion resistance.

Ensure full deployment of the stent (see Section 13.5, Operator's Instructions, Deployment Procedure) and confirm the stent sizing angiographically.

\*Do not exceed the rated burst pressure (RBP).

**15.0 REUSE PRECAUTION STATEMENT**

Do not use if sterile barrier is damaged. If damage is found call your Boston Scientific, Cardiac Therapies representative.

For single patient use only. Do not reuse, reprocess or resterilize.

**16.0 PATENTS**

This product and its use are protected by one or more of the following patents. United States, 4,571,240; 4,573,470; 4,581,017; 4,582,181; 4,597,755; 4,616,653; 4,619,263; 4,638,805; 4,641,654; 4,661,094; 4,664,113; 4,692,200; 4,748,982; 4,771,776; 4,771,777; 4,771,778; 4,775,371; 4,782,834; 4,790,315; 4,793,350; 4,821,722; 4,877,031; 4,892,519; 4,938,220; 4,940,062; 4,964,409; 4,976,720; 4,981,478; 4,998,917; 4,998,923; 5,002,532; 5,002,560; 5,003,989; 5,034,001; 5,040,548; 5,042,985; 5,046,503; 5,061,273; 5,090,959; 5,135,535; 5,137,513; 5,154,725; 5,159,937; 5,176,661; 5,180,368; 5,195,971; 5,234,002; 5,242,394; 5,242,396; 5,256,143; 5,263,963; 5,279,562; 5,290,230; 5,300,025; 5,300,085; 5,316,706; 5,318,527; 5,324,259; 5,334,154; 5,342,621; 5,346,505; 5,348,537; 5,350,395; 5,391,172; 5,397,305; 5,409,495; 5,411,476; 5,415,637; 5,421,955; 5,423,755; 5,423,885; 5,437,083; 5,441,515; 5,443,458; 5,443,500; 5,451,209; 5,451,233; 5,456,667; 5,458,605; 5,458,613; 5,458,615; 5,476,505; 5,480,383; 5,496,275; 5,496,346; 5,498,240; 5,507,301; 5,507,768; 5,507,795; 5,514,154; 5,516,336; 5,525,388; 5,533,968; 5,542,925; 5,546,646; 5,549,551; 5,549,554; 5,554,120; 5,554,121; 5,556,413; 5,558,643; 5,565,523; 5,573,508; 5,573,509; 5,591,197; 5,593,434; 5,603,721; 5,605,696; 5,607,444; 5,618,299; 5,629,077; 5,632,754; 5,632,840; 5,636,641; 5,637,089; 5,637,113; 5,649,977; 5,681,346; 5,693,015; 5,695,506; 5,700,286; 5,707,385; 5,709,658; 5,725,549; 5,728,158; 5,735,893; 5,743,875; 5,747,591; 5,749,888; 5,759,192; 5,769,868; 5,780,807; 5,782,855; 5,807,355; 5,816,923; 5,830,181; 5,849,846; 5,868,706; 5,868,767; 5,891,090; 5,902,290; 5,931,819; 5,989,218; 5,993,460; 6,013,054; 6,013,069; 6,013,728; 6,017,364; 6,019,777; 6,027,475; 6,036,707; 6,036,715;

6,056,776; 6,059,748; 6,059,770; 6,061,588; 6,117,106; 6,126,634; 6,126,635; 6,129,707; 6,131,266; 6,136,011; 6,139,525; 6,156,047; 6,165,152; 6,165,292; 6,179,810; 6,193,686; 6,200,325 B1; 6,206,852; 6,217,547; 6,221,425; 6,224,803; 6,238,376; 6,248,092; 6,251,094; 6,273,911; 6,296,655; 6,299,595; 6,309,412; 6,369,355; 6,419,693; 6,432,133; 6,482,166; 6,485,511; 6,488,655; 6,488,694; 6,527,789; 6,561,788; 6,572,813; 6,575,958; 6,575,993; 6,620,193; 6,629,991; RE 33,166; RE 34,564.

Other U.S. patents pending. Foreign patents issued and pending.

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**Graphical Symbols for Medical Device Labeling**

 Manufacturer	<b>REF</b> Catalogue Number	<b>F</b> French Size
 Do not reuse, do not resterilize	<b>STERILE EO</b> Sterilized using Ethylene Oxide	 Consult Instructions for Use
 Use By	<b>LOT</b> Batch Code	 Date of Manufacture
 Guiding Catheter	<b>PYROGEN</b> Non-Pyrogenic	 Contents (Numeral represents quantity of units inside)
 Inner Diameter		

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**The XIENCE™ V Everolimus Eluting Coronary Stent System**  
**Instructions for Use**



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## 1.0 PRODUCT DESCRIPTION

The XIENCE™ V Everolimus Eluting Coronary Stent System (XIENCE V EECSS or XIENCE V stent system) is a device/drug combination product consisting of either the MULTI-LINK VISION® Coronary Stent System or the MULTI-LINK MINI VISION® Coronary Stent System coated with a formulation containing everolimus, the active ingredient, embedded in a non-erodible polymer.

### 1.1 Device Component Description

The device component consists of the MULTI-LINK MINI VISION or MULTI-LINK VISION stent mounted onto the MULTI-LINK MINI VISION or MULTI-LINK VISION stent delivery system (SDS) respectively. The device component characteristics are summarized in Table 1-1.

**Table 1-1: XIENCE V Stent System Product Description**

	XIENCE V Rapid-Exchange (RX) EECSS	XIENCE V Over-the-Wire (OTW) EECSS																					
Available Stent Lengths (mm)	8, 12, 15, 18, 23, 28	8, 12, 15, 18, 23, 28																					
Available Stent Diameters (mm)	2.5, 2.75, 3.0, 3.5, 4.0	2.5, 2.75, 3.0, 3.5, 4.0																					
Stent Material	A medical grade L-605 cobalt chromium (CoCr) alloy MULTI-LINK VISION or MULTI-LINK MINI VISION stent																						
Drug Component	A conformal coating of a non-erodible polymer loaded with 100 µg/cm <sup>2</sup> of everolimus with a maximum nominal drug content of 181 • g on the large stent (4.0 x 28 mm)																						
Delivery System Working Length	143 cm	143 cm																					
Delivery System Design	Single access port to inflation lumen. Guide wire exit notch is located 30 cm from tip. Designed for guide wires • 0.014".	Sidearm adaptor provides access to balloon inflation/deflation lumen and guide wire lumen. Designed for guide wires • 0.014".																					
Stent Delivery System Balloon	A compliant, tapered balloon, with two radiopaque markers located on the catheter shaft to indicate balloon positioning and expanded stent length.																						
Balloon Inflation Pressure	Nominal inflation pressure: 8 atm (811 kPa) for 2.5 and 2.75 mm diameters; 9 atm (912 kPa) for 3.0, 3.5, and 4.0 mm diameters Rated Burst Pressure (RBP): 16 atm (1621 kPa) for all sizes																						
Guiding Catheter Inner Diameter	• 5 F (0.056")																						
Catheter Shaft Outer Diameter (nominal)	<table><tr><td></td><td><u>2.5–3.0 mm</u></td><td><u>3.5–4.0 mm</u></td></tr><tr><td>Distal:</td><td>0.032"</td><td>0.035"</td></tr><tr><td>Proximal:</td><td>0.026"</td><td>0.026"</td></tr></table>		<u>2.5–3.0 mm</u>	<u>3.5–4.0 mm</u>	Distal:	0.032"	0.035"	Proximal:	0.026"	0.026"	<table><tr><td></td><td><u>2.5 mm</u></td><td><u>2.75 x 8 – 3.5 x 18</u></td><td><u>3.5 x 23 – 4.0 x 28</u></td></tr><tr><td>Distal:</td><td>0.032"</td><td>0.034"</td><td>0.036"</td></tr><tr><td>Proximal:</td><td>0.042"</td><td>0.042"</td><td>0.042"</td></tr></table>		<u>2.5 mm</u>	<u>2.75 x 8 – 3.5 x 18</u>	<u>3.5 x 23 – 4.0 x 28</u>	Distal:	0.032"	0.034"	0.036"	Proximal:	0.042"	0.042"	0.042"
	<u>2.5–3.0 mm</u>	<u>3.5–4.0 mm</u>																					
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Distal:	0.032"	0.034"	0.036"																				
Proximal:	0.042"	0.042"	0.042"																				

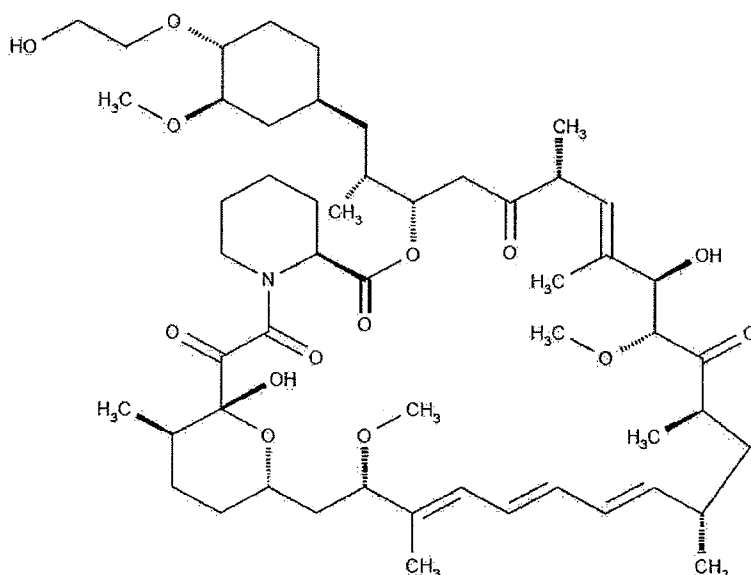
## 1.2 Drug Component Description

The XIENCE V Everolimus Eluting Coronary Stent (XIENCE V stent) is coated with everolimus (active ingredient), embedded in a non-erodible polymer (inactive ingredient).

### 1.2.1 Everolimus

Everolimus is the active pharmaceutical ingredient in the XIENCE V stent. It is a novel semi-synthetic macrolide immunosuppressant, synthesized by chemical modification of rapamycin (sirolimus). The everolimus chemical name is 40-O-(2-hydroxyethyl)-rapamycin and the chemical structure is shown in Figure 1-1 below.

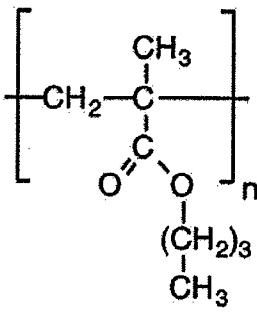
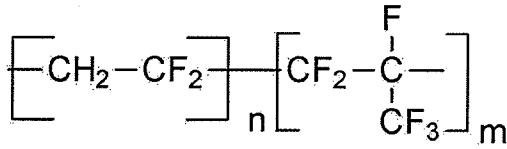
Figure 1-1: Everolimus Chemical Structure



### 1.2.2. Inactive Ingredients – Non-erodible Polymer

The XIENCE V stent contains inactive ingredients including poly n-butyl methacrylate (PBMA), a polymer that adheres to the stent and drug coating, and PVDF-HFP, which is comprised of vinylidene fluoride and hexafluoropropylene monomers as the drug matrix layer containing everolimus. PBMA is a homopolymer with a molecular weight (Mw) of 264,000 to 376,000 dalton. PVDF-HFP is a non-erodible semi-crystalline random copolymer with a molecular weight (Mw) of 254,000 to 293,000 dalton. The drug matrix copolymer is mixed with everolimus (83%/17% w/w polymer/everolimus ratio) and applied to the entire PBMA coated stent surface. The drug load is 100 µg/cm<sup>2</sup> for all product sizes. No topcoat layer is used. The polymer chemical structures are shown in Figure 1-2 below.

Figure 1-2: Non-erodible Polymer Chemical Structures

PBMA	PVDF-HFP
 $\left[ \text{CH}_2 - \underset{\begin{array}{c} \text{O} \\ \parallel \\ \text{C} - \text{O} - (\text{CH}_2)_3 - \text{CH}_3 \end{array}}{\overset{\text{CH}_3}{\text{C}}} \right]_n$	 $\left[ \text{CH}_2 - \text{CF}_2 \right]_n \left[ \text{CF}_2 - \underset{\text{CF}_3}{\overset{\text{F}}{\text{C}}} \right]_m$

### 1.2.3 Product Matrix and Everolimus Content

Table 1-3: XIENCE V EECSS Product Matrix and Everolimus Content

Model Number (RX)	Model Number (OTW)	Nominal Expanded Stent Diameter (mm)	Nominal Unexpanded Stent Length (mm)	Nominal Everolimus Content (µg)
1009539-08	1009545-08	2.5	8	37
1009540-08	1009546-08	2.75	8	37
1009541-08	1009547-08	3.0	8	37
1009542-08	1009548-08	3.5	8	53
1009543-08	1009549-08	4.0	8	53
1009539-12	1009545-12	2.5	12	56
1009540-12	1009546-12	2.75	12	56
1009541-12	1009547-12	3.0	12	56
1009542-12	1009548-12	3.5	12	75
1009543-12	1009549-12	4.0	12	75
1009539-15	1009545-15	2.5	15	75
1009540-15	1009546-15	2.75	15	75
1009541-15	1009547-15	3.0	15	75
1009542-15	1009548-15	3.5	15	98
1009543-15	1009549-15	4.0	15	98
1009539-18	1009545-18	2.5	18	88
1009540-18	1009546-18	2.75	18	88
1009541-18	1009547-18	3.0	18	88
1009542-18	1009548-18	3.5	18	113
1009543-18	1009549-18	4.0	18	113
1009539-23	1009545-23	2.5	23	113
1009540-23	1009546-23	2.75	23	113
1009541-23	1009547-23	3.0	23	113
1009542-23	1009548-23	3.5	23	151
1009543-23	1009549-23	4.0	23	151
1009539-28	1009545-28	2.5	28	132
1009540-28	1009546-28	2.75	28	132
1009541-28	1009547-28	3.0	28	132
1009542-28	1009548-28	3.5	28	181
1009543-28	1009549-28	4.0	28	181

## 2.0 INDICATIONS

The XIENCE V Everolimus Eluting Coronary Stent System (XIENCE V stent) is indicated for improving coronary luminal diameter in patients with symptomatic heart disease due to *de novo* native coronary artery lesions (length • 28 mm) with reference vessel diameters of 2.5 mm to 4.25 mm.

## 3.0 CONTRAINDICATIONS

The XIENCE V stent is contraindicated for use in patients:

- Who cannot receive antiplatelet and/or anti-coagulant therapy (see **Section 5.2 Pre- and Post-Procedure Antiplatelet Regimen** for more information)
- With lesions that prevent complete angioplasty balloon inflation or proper placement of the stent or stent delivery system
- With hypersensitivity or contraindication to everolimus or structurally-related compounds, cobalt, chromium, nickel, tungsten, acrylic, and fluoropolymers

## 4.0 WARNINGS

- Ensure that the inner package sterile barrier has not been opened or damaged prior to use.
- Judicious patient selection is necessary because device use has been associated with stent thrombosis, vascular complications, and/or bleeding events.
- This product should not be used in patients who are not likely to comply with the recommended antiplatelet therapy (see Section 5.2 for important information regarding antiplatelet therapy).

## 5.0 PRECAUTIONS

### 5.1 General Precautions

- Stent implantation should only be performed by physicians who have received appropriate training.
- Stent placement should be performed at hospitals where emergency coronary artery bypass graft surgery is accessible.
- Subsequent restenosis may require repeat dilatation of the arterial segment containing the stent. Long-term outcomes following repeat dilatation of the stent is presently unknown.
- Risks and benefits should be considered in patients with severe contrast agent allergies.
- Care should be taken to control the guiding catheter tip during stent delivery, deployment, and balloon withdrawal. Before withdrawing the stent delivery system, visually confirm complete balloon deflation by fluoroscopy to avoid guiding catheter movement into the vessel and subsequent arterial damage.
- Stent thrombosis is a low-frequency event that current drug-eluting stent (DES) clinical trials are not adequately powered to fully characterize. Stent thrombosis is frequently associated with myocardial infarction (MI) or death. Data from the XIENCE V SPIRIT family of trials have been prospectively evaluated and adjudicated using both the protocol definition of stent thrombosis and the definition developed by the Academic

Research Consortium (ARC), and demonstrate specific patterns of stent thrombosis that vary depending on the definition used (see Section 8.2 Stent Thrombosis Definitions and Section 9.4 SPIRIT II and SPIRIT III Pooled Analysis, for more information). In the XIENCE V SPIRIT family of trials analyzed to date, the differences in the incidence of stent thrombosis observed with the XIENCE V stent compared to the TAXUS stent have not been associated with an increased risk of cardiac death, MI, or all-cause mortality. Additional data from longer-term follow-up in the XIENCE V SPIRIT family of trials and analyses of DES-related stent thrombosis are expected and should be considered in making treatment decisions as data become available.

- When DES are used outside the specified Indications for Use, patient outcomes may differ from the results observed in the XIENCE V SPIRIT family of trials.
- Compared to use within the specified Indications for Use, the use of DES in patients and lesions outside of the labeled indications, including more tortuous anatomy, may have an increased risk of adverse events, including stent thrombosis, stent embolization, MI, or death.
- Orally administered everolimus combined with cyclosporine is associated with increased serum cholesterol and triglycerides levels.

## 5.2 Pre- and Post-Procedure Antiplatelet Regimen

- In XIENCE V SPIRIT FIRST clinical trial, clopidogrel bisulfate or ticlopidine hydrochloride was administered pre-procedure and for a minimum of 3 months post-procedure (75 mg per day). In XIENCE V SPIRIT II and SPIRIT III clinical trials, clopidogrel bisulfate or ticlopidine hydrochloride was administered pre-procedure and for a minimum of 6 months post-procedure (75 mg per day). Aspirin was administered (a minimum of 75 mg per day) pre-procedure and continued for 1 to 5 years (depending on the study). Based on the case report forms from the SPIRIT II and III randomized clinical trials, approximately 92% of patients remained on dual antiplatelet therapy at 6 months and 62% at 1 year. See Section 9.0 – Clinical Studies, for more specific information.
- The optimal duration of dual antiplatelet therapy, specifically clopidogrel, is unknown and DES thrombosis may still occur despite continued therapy. Data from several studies on sirolimus-eluting or paclitaxel-eluting stents suggest that a longer duration of clopidogrel than was recommended post-procedurally in DES pivotal trials may be beneficial. Current guidelines recommend that patients receive aspirin indefinitely and that clopidogrel therapy be extended to 12 months in patients at low risk of bleeding (ref: ACC/AHA/SCAI PCI Practice Guidelines<sup>1,2</sup>).
- It is very important that the patient is compliant with the post-procedural antiplatelet therapy recommendations. Early discontinuation of prescribed antiplatelet medication could result in a higher risk of thrombosis, MI, or death. Prior to percutaneous coronary intervention (PCI), if the patient is required to undergo a surgical or dental procedure that might require early discontinuation of antiplatelet therapy, the interventionalist and patient should carefully consider whether a DES and its associated recommended antiplatelet therapy is the appropriate PCI treatment of choice. Following PCI, should a surgical or dental procedure be recommended that requires suspension of antiplatelet therapy, the risks and benefits of the procedure should be weighed against the possible risks associated with early discontinuation of antiplatelet therapy. Patients who require early discontinuation of antiplatelet therapy (e.g., secondary to active bleeding) should

<sup>1</sup> Smith et al. ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention. JACC, 2006; 47: e1-121

<sup>2</sup> King III et al. 2007 Focused Update of the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention. JACC, 2008; 51:172-209

be monitored carefully for cardiac events. At the discretion of the patient's treating physicians, the antiplatelet therapy should be restarted as soon as possible.

### **5.3 Multiple Stent Use**

A patient's exposure to drug and polymer is proportional to the number and total length of implanted stents. In the SPIRIT II and III clinical trials, treatment was limited to 36 mm of total stent length in up to two lesions in different epicardial vessels. Use of more than two stents to treat lesions longer than 28 mm has not been evaluated and may increase patient complication risks. Studies evaluating the effects of higher drug doses have not been conducted.

Effects of multiple stenting using XIENCE V stents combined with other drug-eluting stents are also unknown. When multiple drug-eluting stents are required, use only XIENCE V stents in order to avoid potential interactions with other drug-eluting or coated stents.

In addition, only stents composed of similar materials should be implanted in consecutive stent to stent contact to avoid corrosion potential between unrelated materials. Although *in vitro* tests combining L-605 CoCr alloy with 316 L stainless steel did not increase corrosion potential, these studies have not been conducted *in vivo*.

### **5.4 Brachytherapy**

XIENCE V stent safety and effectiveness has not been evaluated in patients with prior target lesion or in-stent restenosis-related brachytherapy.

### **5.5 Use in Conjunction with Other Procedures**

The safety and effectiveness of using mechanical atherectomy devices (directional atherectomy catheters, rotational atherectomy catheters) or laser angioplasty catheters in conjunction with XIENCE V stent implantation have not been established.

### **5.6 Use in Special Populations**

#### **5.6.1 Pregnancy**

Pregnancy Category C. See Section 6.5 – Drug Information, Pregnancy. The XIENCE V stent has not been tested in pregnant women or in men intending to father children. Effects on the developing fetus have not been studied. Effective contraception should be initiated before implanting a XIENCE V stent and continued for one year after implantation. While there is no contraindication, the risks and reproductive effects are unknown at this time.

#### **5.6.2 Lactation**

See Section 6.6 – Drug Information, Lactation. A decision should be made whether to discontinue nursing prior to stent implantation considering the importance of the stent to the mother.

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### **5.6.3 Gender**

No safety- or effectiveness-related gender differences were observed in the individual XIENCE V clinical trials.

### **5.6.4 Ethnicity**

Insufficient subject numbers prevent ethnicity-related analyses on XIENCE V safety and effectiveness.

### **5.6.5 Pediatric Use**

Safety and effectiveness of the XIENCE V stent in pediatric subjects have not been established.

### **5.6.6 Geriatric Use**

Clinical studies of the XIENCE V stent did not suggest that patients age 65 years and over differed with regard to safety and effectiveness compared to younger patients.

## **5.7 Lesion/Vessel Characteristics**

Safety and effectiveness of the XIENCE V stent have not been established for subject populations with the following clinical settings:

- Unresolved vessel thrombus at the lesion site
- Coronary artery reference vessel diameters < 2.5 mm or > 4.25 mm
- Lesion lengths > 28 mm
- Lesions located in saphenous vein grafts
- Lesions located in unprotected left main coronary artery, ostial lesions, chronic total occlusions, lesions located at a bifurcation
- Previously stented lesions
- Diffuse disease or poor flow (TIMI < 1) distal to the identified lesions
- Excessive tortuosity proximal to or within the lesion
- Recent acute myocardial infarction (AMI) or evidence of thrombus in the target vessel
- Moderate or severe lesion calcification
- Multivessel disease
- In-stent restenosis
- Patients with longer than 24 months follow-up.

## **5.8 Drug Interactions**

See Section 6.3 – Drug Information, Interactions with Drugs or Other Substances. Several drugs are known to affect everolimus metabolism, and other drug interactions may also occur. Everolimus is known to be a substrate for both cytochrome P4503A4 (CYP3A4) and P-glycoprotein. Everolimus absorption and subsequent elimination may be influenced by drugs that affect these pathways. Everolimus has also been shown to reduce the clearance of some prescription medications when administered orally along with cyclosporine (CsA). Formal drug interaction studies have not been performed with the XIENCE V stent because of limited systemic exposure to everolimus eluted from XIENCE V (see Section 6.2 Pharmacokinetics).

Therefore, due consideration should be given to the potential for both systemic and local drug interactions in the vessel wall when deciding to place the XIENCE V stent in a patient taking a drug with known interaction with everolimus, or when deciding to initiate therapy with such a drug in a patient who has recently received a XIENCE V Stent.

## 5.9 Immune Suppression Potential

Everolimus, the XIENCE V stent active ingredient, is an immunosuppressive agent. Immune suppression was not observed in the XIENCE V clinical trials. However, for patients who receive several XIENCE V stents simultaneously, it may be possible for everolimus systemic concentrations to approach immunosuppressive levels temporarily, especially in patients who also have hepatic insufficiency or who are taking drugs that inhibit CYP3A4 or P-glycoprotein. Therefore, consideration should be given to patients taking other immunosuppressive agents or who are at risk for immune suppression.

## 5.10 Lipid Elevation Potential

Oral everolimus use in renal transplant patients was associated with increased serum cholesterol and triglycerides that in some cases required treatment. The effect was seen with both low and high dose prolonged oral therapy in a dose related manner. When used according to the indications for use, exposure to systemic everolimus concentrations from the XIENCE V stent are expected to be significantly lower than concentrations usually obtained in transplant patients. Increased serum cholesterol and triglycerides were not observed in the XIENCE V SPIRIT family of clinical trials.

## 5.11 Magnetic Resonance Imaging (MRI)

Non-clinical testing has demonstrated that the XIENCE V stent, in single and in overlapped configurations up to 68 mm in length, is MR Conditional. It can be scanned safely under the following conditions:

- Static magnetic field of 1.5 or 3 Tesla
- Spatial gradient field of 720 Gauss/cm or less
- Maximum whole-body-averaged specific absorption rate (SAR) of 2.0 W/kg (normal operating mode) for 15 minutes of scanning or less

The XIENCE V stent should not migrate in this MRI environment. Non-clinical testing at field strengths greater than 3 Tesla has not been performed to evaluate stent migration or heating. MRI at 1.5 or 3 Tesla may be performed immediately following the implantation of the XIENCE V stent.

Stent heating was derived by relating the measured non-clinical, *in vitro* temperature rises in a GE Excite 3 Tesla scanner and in a GE 1.5 Tesla coil to the local specific absorption rates (SARs) in a digitized human heart model. The maximum whole body averaged SAR was determined by validated calculation. At overlapped lengths up to 68 mm, the XIENCE V stent produced a non-clinical maximum local temperature rise of 3°C at a maximum whole body averaged SAR of 2.0 W/kg (normal operating mode) for 15 minutes. These calculations do not take into consideration the cooling effects of blood flow.

The effects of MRI on overlapped stents greater than 68 mm in length or stents with fractured struts are unknown.

As demonstrated in non-clinical testing, an image artifact can be present when scanning the XIENCE V stent. MR image quality may be compromised if the area of interest is in the exact same area, or relatively close to, the position of the XIENCE V stent. Therefore, it may be necessary to optimize the MR imaging parameters for the presence of XIENCE V stents.

## 5.12 Stent Handling

- **Each stent is for single use only.** Do not resterilize or reuse this device. Note the "use by" (expiration) date on the product label.
- **The foil pouch is not a sterile barrier.** The inner header bag (pouch) within the foil pouch is the sterile barrier. Only the contents of the inner pouch should be considered sterile. The outside surface of the inner pouch is NOT sterile.
- **Do not remove the stent from the delivery system.** Removal may damage the stent and/or lead to stent embolization. These components are intended to perform together as a system.
- The delivery system should not be used in conjunction with other stents.
- Special care must be taken not to handle or disrupt the stent on the balloon especially during delivery system removal from packaging, placement over the guide wire and advancement through the rotating hemostatic valve adapter and guiding catheter hub.
- **Do not manipulate, touch, or handle the stent** with your fingers, which may cause coating damage, contamination, or stent dislodgement from the delivery balloon.
- Use only the appropriate balloon inflation media (see Section 13.3.3 – Operator's Instructions, Delivery System Preparation). Do not use air or any gaseous medium to inflate the balloon as this may cause uneven expansion and difficulty in stent deployment.

## 5.13 Stent Placement

### 5.13.1 Stent Preparation

- **Do not prepare or pre-inflate the delivery system prior to stent deployment other than as directed.** Use the balloon purging technique described in Section 13.3.3 – Operator's Instructions, Delivery System Preparation.
- **Do not induce negative pressure on the delivery system prior to placing the stent across the lesion.** This may cause dislodgement of the stent from the balloon.
- Use guiding catheters which have lumen sizes that are suitable to accommodate the stent delivery system (see Section 1.1 – Product Description, Device Component Description).

### 5.13.2 Stent Implantation

- The vessel should be pre-dilated with an appropriate sized balloon. Failure to do so may increase the difficulty of stent placement and cause procedural complications.
- Do not expand the stent if it is not properly positioned in the vessel (see Section 5.14 – Precautions, Stent System Removal).
- Implanting a stent may lead to vessel dissection and acute closure requiring additional intervention (CABG, further dilatation, placement of additional stents, or other).
- Although the safety and effectiveness of treating more than one vessel per coronary artery with XIENCE V stents has not been established, if this is performed, place the

stent in the distal lesion before the proximal lesion in order to minimize dislodgement risk incurred by traversing through deployed stents.

- Stent placement may compromise side branch patency.
- **Do not exceed Rated Burst Pressure (RBP) as indicated on product label.** See Table 14-1, Typical XIENCE V EECSS Compliance. Balloon pressures should be monitored during inflation. Applying pressures higher than specified on the product label may result in a ruptured balloon with possible arterial damage and dissection. The stent inner diameter should approximate 1.1 times the reference diameter of the vessel.
- An unexpanded stent may be retracted into the guiding catheter one time only. An unexpanded stent should not be reintroduced into the artery once it has been pulled back into the guiding catheter. Subsequent movement in and out through the distal end of the guiding catheter should not be performed as the stent may be damaged when retracting the undeployed stent back into the guiding catheter.
- Should **any resistance** be felt at **any time** during coronary stent system withdrawal, the stent delivery system and guiding catheter should be **removed as a single unit** (see Section 5.14 – Precautions, Stent System Removal).
- Stent retrieval methods (i.e., using additional wires, snares, and/or forceps) may result in additional trauma to the coronary vasculature and/or the vascular access site. Complications may include bleeding, hematoma, or pseudoaneurysm.
- Although the stent delivery system balloon is strong enough to expand the stent without rupture, a circumferential balloon tear distal to the stent and prior to complete stent expansion, could cause the balloon to become tethered to the stent, requiring surgical removal. In case of balloon rupture, it should be withdrawn and, if necessary, a new dilatation catheter exchanged over the guide wire to complete the expansion of the stent.
- Ensure the stented area covers the entire lesion/dissection site and that no gaps exist between stents.

#### 5.14 Stent System Removal

Should **any resistance** be felt at **any time** during either lesion access or removing the delivery system post-stent implantation, the stent delivery system and the guiding catheter should be **removed as a single unit**.

**When removing the delivery system and guiding catheter as a single unit, the following steps should be executed under direct visualization using fluoroscopy:**

- Confirm complete balloon deflation. If unusual resistance is felt during stent delivery system withdrawal, pay particular attention to the guiding catheter position. In some cases it may be necessary to slightly retract the guiding catheter in order to prevent unplanned guiding catheter movement and subsequent vessel damage. In cases where unplanned guiding catheter movement has occurred, a coronary tree angiographic assessment should be undertaken to ensure that there is no damage to the coronary vasculature.
- DO NOT retract the delivery system into the guiding catheter.
- Position the proximal balloon marker just distal to guiding catheter tip.
- Advance the guide wire into the coronary anatomy as far distally as safely possible.
- Tighten the rotating hemostatic valve to secure the delivery system to the guiding catheter, and remove the guiding catheter and delivery system as a **single unit**.

Failure to follow these steps and/or applying excessive force to the delivery system can potentially result in loss or damage to the stent and/or delivery system components.

If it is necessary to retain guide wire position for subsequent artery/lesion access, leave the guide wire in place and remove all other system components.

Stent retrieval methods (i.e., additional wires, snares and/or forceps) may result in additional trauma to the coronary vasculature and/or the vascular access site. Complications may include, but are not limited to, bleeding, hematoma, or pseudoaneurysm.

### **5.15 Post-Procedure**

- When **crossing a newly deployed stent** with an intravascular ultrasound (IVUS) catheter, a coronary guide wire, a balloon catheter or delivery system, exercise care to avoid disrupting the stent placement, apposition, geometry, and/or coating.
- Antiplatelet therapy should be administered post-procedure (see Section 5.2 Pre- and Post-Procedure Antiplatelet Regimen and Section 9.0 Clinical Studies). Patients who require early discontinuation of antiplatelet therapy (e.g., secondary to active bleeding) should be monitored carefully for cardiac events. At the discretion of the patient's treating physician, the antiplatelet therapy should be restarted as soon as possible.
- If the patient requires imaging, see Section 5.11 – Precautions, Magnetic Resonance Imaging (MRI).

## **6.0 DRUG INFORMATION**

### **6.1 Mechanism of Action**

The mechanism by which the XIENCE V Stent inhibits neointimal growth as seen in pre-clinical and clinical studies has not been established. At the cellular level, everolimus inhibits growth factor-stimulated cell proliferation. At the molecular level, everolimus forms a complex with the cytoplasmic protein FKBP-12 (FK 506 Binding Protein). This complex binds to and interferes with FRAP (FKBP-12 Rapamycin Associated Protein), also known as mTOR (mammalian Target Of Rapamycin), leading to inhibition of cell metabolism, growth, and proliferation by arresting the cell cycle at the late G1 stage.

### **6.2 Pharmacokinetics of the XIENCE V Everolimus Eluting Coronary Stent**

Everolimus pharmacokinetics (PK) when eluted from the XIENCE V Stent post-implantation has been evaluated in three different substudies in three different geographies. The SPIRIT III clinical trial design includes a pharmacokinetic substudy in the US randomized arm and a pharmacokinetic substudy in the Japanese non-randomized arm. The third PK substudy was conducted as part of the SPIRIT II clinical trial at sites in Europe, India, and New Zealand. Whole blood everolimus PK parameters determined from subjects receiving the XIENCE V stent are provided in Table 6-1.